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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,650	04/02/2001	Masato Nagaoka	01192/HG	3324

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EXAMINER

MAIER, LEIGH C

ART UNIT PAPER NUMBER

1623

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/806,650

**Applicant(s)**

NAGAOKA ET AL.

**Examiner**

Leigh C. Maier

**Art Unit**

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) 6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>9</u> .   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 1, 5, and 7 have been amended. Claim 6 has been withdrawn as being drawn to a non-elected invention. Claims 1-5 and 7 are pending. Any objection or rejection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 U.S.C. § 103***

Claims 1-3 and 7 are again rejected under 35 U.S.C. 103(a) as being unpatentable over DOMB et al (US 6,011,008) in view of JOSEPHSON et al (US 5,336,506), as set forth in the previous Office action.

Independent claim 1 has been amended to require attachment of the antibacterial agent at the reducing end of the (oligo/poly)saccharide.

Applicant's arguments filed September 29, 2003 have been fully considered but they are not persuasive.

Applicant first addresses structural aspects of the DOMB conjugate stating that it does not comprise a sulfated polysaccharide. This was acknowledged in the previous Office action. See page 5, third full paragraph. Applicant further alleges that it is "an unstable chemical compound in which mitomycin is bonded to the hydroxyl groups of the structural sugar of the oxidized arabinogalactan" as opposed to the present invention that "has a chemical structure in which an antibacterial substance is chemically bonded to the reduced end sugar. . ." The

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examiner respectfully disagrees with this characterization of the DOMB product. The mitomycin is attached via a primary amino group to a carbon derived from an aldehyde group. The aldehyde depicted is not at the reducing end, but this point was also addressed previously. In the absence of unexpected results, the conjugation process would not be expected to be limited to reaction at internal aldehydes but would also occur at the reducing end. It is noted that these allegedly “unstable compounds” are stable when purified and suitable for parenteral administration. See col 1, lines 49-67.

With regard to the activity of the DOMB conjugate, Applicant contends that the reference does not teach “how to increase the medicinal stability and antibacterial effect of the drug as well as specific affinity for *Helicobacter pylori* on gastric wall.” In response to applicant’s argument that the references fail to show certain features of applicant’s invention, it is noted that the features upon which applicant relies (i.e., increased stability, specific affinity) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). It may be that the claimed conjugates have unexpectedly high affinity for *H. pylori*, but no evidence to this effect has been submitted.

Applicant also objects to JOSEPHSON because the reference does not teach the claimed sulfated (oligo/poly)saccharide conjugate in which the active agent “is bonded to the reduced end sugar of the sulfated polysaccharide to enhance the specific affinity for *Helicobacter pylori* on the gastric wall while maintaining the medicinal stability and antibacterial effect of the drug.” Applicant appears to be arguing a claim drawn a method of enhancing the activity of an antibacterial substance when what is actually claimed is the product itself. The examiner agrees

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that the reference does not teach every limitation of the claim, but if the reference is used in combination with another reference and was used only to teach that fucoidan is a functional equivalent of arabinogalactan for the delivery of therapeutic agents.

Applicant further contends that the therapeutic agent is attached via an amide or ester linkage. The examiner agrees that it is DOMB and not JOSEPHSON that teaches the type of attachment recited in the claims. It would be obvious to substitute fucoidan in the DOMB procedure to arrive at the type of conjugate of the instant invention.

Claims 1-3 and 7 are again rejected under 35 U.S.C. 103(a) as being unpatentable over DOMB et al (US 6,011,008) in view of JOSEPHSON et al (US 5,336,506) in further view of DADEY (WO 97/37680), as set forth in the previous Office action.

The claims have been amended as set forth above.

Applicant's arguments filed September 29, 2003 have been fully considered but they are not persuasive. The arguments with regard to DOMB and JOSEPHSON have been addressed above.

Applicant contends that the composition disclosed by DADEY is not the same in structure or purpose as the instant invention. The examiner agrees that the rejection was not one of anticipation. Applicant further argues that the suggestion of using sulfated polysaccharides would only apply to conjugation with insulin. The examiner disagrees with this characterization and maintains that one of ordinary skill would see this as a general teaching for the use of sulfated polysaccharides in drug delivery. The examiner also maintains that one of ordinary skill would be motivated to substitute any polysaccharide known to have utility for drug delivery to

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prepare conjugates as taught by DOMB. The fact that the reference does not teach *Helicobacter pylori* affinity has been addressed above.

Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over DOMB et al (US 6,011,008) in view of JOSEPHSON et al (US 5,336,506), and further in view of BORODY (US 5,476,669).

DOMB and JOSEPHSON teach as set forth in the previous Office action. DOMB teaches the use of antibiotics for the therapeutic agent in the conjugate. The references do not specifically teach the preparation of a conjugate comprising an agent having utility for the treatment of gastric ulcers.

BORODY teaches the treatment of ulcers associated with *Helicobacter pylori* by administration of antibiotics, such as penicillins and tetracycline. See abstract.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare the conjugates taught by the combination of DOMB and JOSEPHSON using any known antibiotic, such as penicillin or tetracycline, as DOMB had suggested their use. One of ordinary skill would be motivated to prepare these particular conjugates to treat ulcers associated with *Helicobacter pylori*. The artisan would reasonably expect success in such a method.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

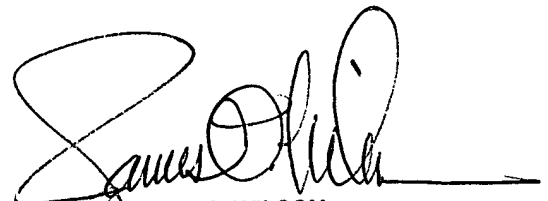
***Examiner's hours, phone & fax numbers***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Wednesday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Leigh C. Maier  
Patent Examiner  
February 27, 2004

  
JAMES O. WILSON  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600